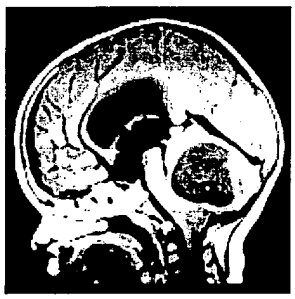

The University of Oklahoma

Health Sciences Center

DEPARTMENT OF NEUROSURGERY

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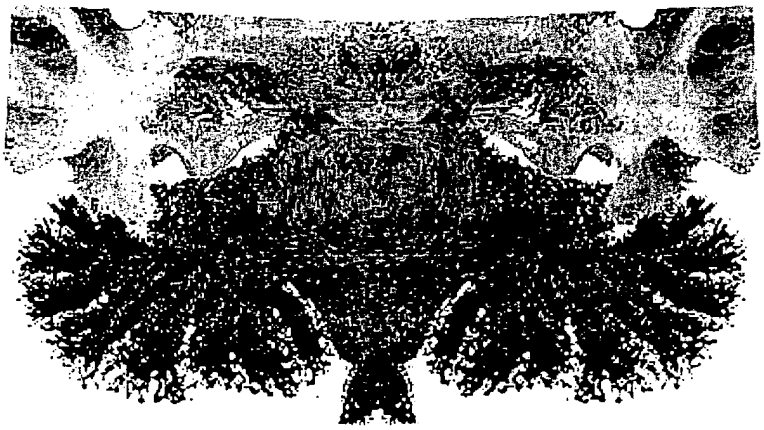

Current Research Projects in the Department Laboratories

- Relationship Between Spinal Motion and Neurologic Deficit in Cervical Spondylotic Myelopathy
  - Cervical spondylotic myelopathy (CSM) is a common condition in which there is narrowing of the spinal canal in the neck, usually due arthritis, multiple herniated discs, or bone spurs. As a result, patients begin losing movement and feeling in their arms and legs. Various

treatments are performed for this problem, the most common of whic is surgery. Multiple surgical options are currently available, though a address different aspects of the problem. Unfortunately, treatment failures are common.
Treatment of patients with CSM could potentially be improved by a better understanding of the disease process. Though we know that th cervical spinal canal is narrowed in CSM, we do not know how this causes loss of movement and feeling. Laboratory experiments have shown that more spinal cord compression is required to recreate CSM than is usually present in the patients that come to surgery. This suggests that there may be some other important factor involved.
In addition to the spinal cord compression present at rest, we know tl the spinal cord is stretched and further compressed each time the nec is moved. Though long term experiments have shown that this movement may be important, no detailed experiments have been don to investigate this.
The purpose of this project is to determine the relationship between spinal motion and the neurological deficits (weakness and loss of feeling) seen in CSM. In order to do this, we plan to recreate the spir canal narrowing seen in the human condition in the cat cervical spine Using the information obtained during the experiment, we will be ab to determine how important spinal motion is in producing the weakn and loss of feeling seen in CSM. This information, in turn, will help decide with some objectivity what the best treatment is for our patier Research done under the direction of Christopher E.Wolfla, M.D..

- The Involvement of Bradykinin in the Pathology of Cerebral Trau
  - Bradykinin is a member of the family of peptide hormones known as kinins having a variety of physiological and pathophysiological effec Bradykinin is recognized as a potent stimulator of pain and is genera in response to cellular injury. In addition, bradykinin is a potent vasodilator. The presence of a kinin system in the **brain** has been established. It is proposed that the kinins and bradykinin, in particula play an important role in the cerebrovascular pathophysiology resulti from cerebral trauma. The project will investigate the role of bradykinin in a fluid percussion head cerebral trauma model. Using a closed cranial window, cerebral pial vessel diameter will be monitor continuously during fluid percussion of injury. Impact pressure will l varied. Specific antagonists to bradykinin will be used to attenuate it vasodilatory effect. Continuing studies will evaluate the involvement systems activated by bradykinin, i.e. arachidonic acid cascade, excitatory amino acids, nitric oxide, in the pathophysiology of head injury. Techniques used in the project include laser Doppler flowmet closed cranial window, and PC based video imaging with morphometric measurement of vessel diameter. Research done under the direction of Paul C. Francel, M.D., Ph.D..

- Conduit Assisted Regeneration of Peripheral Nerves
  - Long nerve gaps continue to a difficult problem for the peripheral nerve surgeon. The present gold standard is an interposed nerve autograft placed to assure the anatomic integrity of the proximal nerv to the distal degenerating nerve. The regenerating nerves progress along the nerve graft scaffold and into the remains of the distal nerve reinnervate the distal motor end plates or sensory organs. The is accomplished at the cost of potential donor site complications includ numbness, painful neuroma formation and unacceptable scarring. Conduit repairs have been attempted to avoid these donor complications. The conduits used have included synthetic materials, autologous artery and vein, and muscle. To date no satisfactory cond has been found. Previous work by Dr. Francel has documented the utility of a silastic conduit in promoting sciatic nerve growth over ga up to 1.5cm, a distance that precludes non-assisted regeneration. Thi project will evaluate the utility of a commercially available, bioresorbable material for use as a conduit in the sciatic nerve injury model. The project will evaluate groups including no implant, autologous nerve implant, silastic conduit implant and bioresorbable implant. In addition to the potential value in peripheral nerve regeneration, these studies will supply information useful in assisting regeneration of central nervous system tissues. Techniques involved include peripheral nerve surgery, lesion generation, conduit implantation, tissue harvest, and tissue preparation for histologic evaluation of nerve regeneration. Research done under the direction Paul C. Francel, M.D., Ph.D..

- Shunt Valve Function in Relation to Placement
  - A variety of shunt valve systems have been devised with siphon-control (SCD) devices designed to prevent overdrainage of cerebrospinal fluid. To date, no compelling evidence has been presented to document the utility of these devices. Estimates of overdrainage are reported in the range of 30%. When reviewing the product literature with regard to surgical placement of these devices, there is a recommendation that the valve- SCD assemble be placed a the level of the inlet catheter tip. Placement above this level will resu in higher intra-ventricular pressures and slower than specified outflo rates, and placement of the assemble below this level will result in lower intra-ventricular pressures with higher than specified outflow rates. It is our proposal that valve placement with regard to inlet catheter tip is absolutely essential for proper function of the valve. Tl project will evaluate, on the bench, a variety of shunt valve types fro a number of manufacturers. Valves will be positioned such that they are flowing at a nominal rate of 50ml/hr by adjusting the starting hea pressure. Lower resistance valves will require a lower head pressure attain this flow rate. The position of the inlet catheter tip will be fixe at this 0 level, and the valve-SCD will be moved in relation to the inl tip. Both positive and negative offsets will be used. Preliminary

evidence has shown that elevating the valve-SCD above the inlet tip results in a significant reduction of outflow. Movement of the valve below the level of the inlet tip results in significant increases in outfl rate. The changes in outflow rate are proportional to the distance between the valve assembly and the inlet catheter tip. The net effect moving the valve with respect to the inlet tip is to alter the head pressure on the inlet side of the valve, thereby controlling flow in a pressure dependent fashion. Research done under the direction of Pa C. Francel, M.D., Ph.D..

- Delivery of **Doxorubicin** (Adriamycin) to the **Brain** for Treatmen of Tumors
  - **Doxorubicin** is an effective chemotherapeutic drug for breast cancer Since 17% of all breast cancer patients experience metastases to the **brain**, **doxorubicin** could be potentially useful in the treatment of these tumors. However, **doxorubicin**, even in low dose, is highly neurotoxic, precluding it's use for tumors of this nature. Recent development of drug encapsulation in sterically stabilized liposomes (Stealth Liposomes) offers hope of avoiding high tissue levels of fre drug to attain therapeutic concentrations. The liposomes serve as a second compartment for the drug, releasing it slowly to the tissue, significantly increasing the plasma and tissue half-life of the drug. Although penetration of **doxorubicin** and liposome encapsulated **doxorubicin** into the **brain** is prevented by the intact blood-**brain** barrier, we have been using hyperosmotic blood-**brain** barrier disruption to effect delivery of normally excluded agents to the **brai** parenchyma. This study is designed to investigate the penetration an distribution of both free and liposomal encapsulated **doxorubicin** in normal **brain** following blood-**brain** barrier disruption. The continuation of these studies involves determination of the kinetics o **doxorubicin** in **brain** and evaluation of the neurotoxicity of the encapsulated drug. Techniques include blood-**brain** barrier disruptio and scanning confocal laser microfluorometry for detection of **doxorubicin** autofluorescence. Research done under the direction of Mary K. Gumerlock, M.D.

Current Clinical Research Projects

- BBBD - Blood **Brain** Barrier Disruption Study
  - This study has four specific aims:
    - To evaluate the efficacy between post-operative focal cranial irradiation followed by combination chemotherapy (intraarteri methotrexate and intravenous cytoxan) with BBBD (Arm I) an postoperative combination chemotherapy (intraarterial

methotrexate and intravenous cytoxan) with BBBD followed b focal cranial radiation (Arm II)

- The second goal is to evaluate differences in tumor response, i any, between patients in Arm I and Arm II.
- The third goal is to assess patient clinical and cognitive functic and evaluate and compare treatment related neurotoxicity, if a in each ARM and between the ARMS through serial neuropsychologic testing and radiographic imaging.
- The fourth goal is to prospectively evaluate the differences in response, survival, and function, if any, between patients undergoing initial tumor diagnosis by biopsy or surgical resection.

- BAK/C Interbody Fusion Study
  - The purpose of this study is to determine the safety and effectiveness the BAK/C Interbody Systen as compared to an uninstrumented ACI (anterior cervical discectomy with fusion) for one and two level disease. Patients fitting inclusion criteria will be randomized into thr groups. The three groups are BAK/C, BAK/C with a hydroxyapetite coating, and uninstrumented ACDF. The BAK/C interbody fusion system consists of square-threaded, hollow, titanium alloy cylinders with openings to allow for bone growth through the device.

This Page was last updated November 3, 1998